Verbal episodic memory in children undergoing temporal lobe epilepsy surgery: a one-year follow-up study

Enric Bellido-Castillo, Anna López-Sala, Javier Aparicio, Daniel Cuadras, Andrea Palacio-Navarro

Introduction. Verbal episodic memory (VEM) is often unimpaired in children with focal epilepsy undergoing left temporal lobe resections, unlike what we might expect in the adult brain. The latter findings suggest that epileptiform activity in early life disrupts memory system lateralization, leading to the development of bilateral memory representation. The present study aims to analyze whether the laterality of epilepsy is a major predictor for post-operative VEM prognosis in pediatric temporal lobe epilepsy (TLE) surgery. This research also pretends to provide evidence about the relationship of VEM performance with other relevant demographical and clinical factors such as sex, age at onset of seizures, age at surgery and duration of epilepsy, as well as to study the impact of presurgical VEM performance on postsurgical outcomes.

Patients and methods. Pre-operative and one-year follow-up post-operative word-list recall scores from 25 children who underwent TLE surgery (left-sided, $n = 11$; right-sided, $n = 14$) were extracted from the Hospital Sant Joan de Déu database and were retrospectively analyzed.

Results. No significant presurgical intergroup differences were found when comparing VEM scores by laterality of epilepsy ($p > 0.5$). Looking at the left TLE group, a high negative correlation was found between the onset age and the pre-operative long-term free recall score (rho = –0.72, $p = 0.01$). No significant pre- to post-operative intragroup changes were found regarding VEM performance, regardless of epilepsy laterality (left TLE group, $p > 0.56$; right TLE group, $p > 0.12$).

Conclusions. The laterality of epilepsy does not show to be a significant factor in and of itself regarding presurgical VEM outcome and its prognosis one year after surgery, thus supporting the bilateral memory representation hypothesis. Furthermore, a younger age at onset of seizures seems to be related with a better pre-operative VEM performance, likely due to a more efficient reorganization of memory system induced by a greater brain plasticity at lower ages; however, this relationship has been only reported for the left-sided epilepsies in our sample.

Key words. Drug resistant epilepsy. Episodic memory. Neuronal plasticity. Neurosurgery. Pediatric hospitals. Temporal lobe epilepsy.

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Introduction

The onset of any disease that affects brain development, at a stage of constant maturation such as childhood, is strongly related to neuropsychological impairments [1,2] and has a great impact on the cognitive, social, behavioral and emotional domain of children [2].

The prevalence of epilepsy goes from 0,8 to 1,2%, represents one of the most common chronic diseases, affecting a total of 50 million people worldwide [3]. In children, epilepsy is the most common chronic neurological disorder, with an annual incidence of approximately 62,6 cases per 100,000 children [4].

The 70% of the pediatric epileptic population respond well to good clinical management, with medical treatment, through the administration of antiseizure medications [5]. The remaining 30% become drug-refractory epilepsies and therefore possible candidates for epilepsy surgery. The aim of early surgical intervention is to optimize the developmental trajectory of children and adolescents with epilepsy, and it is possible that successful surgical intervention, cessation of seizures and reduction of pharmacotherapy may enhance cognitive development [6]. Overall, two thirds of children who undergo epilepsy surgery remain seizure-free in the long-term [7].

Benova et al [3] describe some factors that might affect the cognitive performance of epileptic patients, such as age at onset, duration of epilepsy, location of seizure focus and the administration of antiseizure medications. An early onset age is asso-

ciated with a poorer cognitive performance in numerous studies [8-12]. Moreover, it has been described that children with an epilepsy duration longer than four years present cognitive deficits more frequently than those with shorter epilepsies [13]. Regarding the seizure focus location, temporal lobe origin epilepsies are also known to have better cognitive prognosis than extratemporal or multifocal epilepsies [14]. The administration of antiseizure medications may cause impairment in working memory and information processing speed, especially in combined administrations [15-17].

The temporal lobe plays a prominent role in declarative memory function, including episodic memory [6]. We already know that the perirhinal, entorhinal and parahippocampal cortexes, together with the hippocampus, form the key components of an integrated temporal lobe memory system [18]. More recently, in their study, Meekes et al [19] also state that the left hippocampus is crucial for verbal episodic memory (VEM). That's why some authors state that VEM impairment is a prevalent cognitive disturbance in children with temporal lobe epilepsy (TLE), likely due to the significant involvement of temporomesial structures in memory processing and the negative impact of recurrent seizures on hippocampal dendritic growth [20].

The importance of the dominant hemisphere (usually, the left cerebral hemisphere) is well known for the development of linguistic functions [21]. However, when epilepsy affects an immature, vulnerable, developing brain, it may cause significant alterations in the classical location of brain functions, therefore we know that there is no such predominance or it may be perfectly transferred or divided in patients with early onset epilepsy. This diversity of possible reorganization patterns complicates the assessment of the role played by each hemisphere in language in patients with focal lesions [22]. The fact that VEM is not always impaired in left temporal lobe resections in children suggests that, just as happens with language functions, epileptogenic activity in early life leads to the development of bilateral memory representation due to the disordered or disrupted organization of the memory lateralization system [20].

Surgical resection for medication-resistant and well-localized TLE has a good prognosis for freedom from seizures, but is linked to memory difficulties in adults, especially when the removal is on the language dominant hemisphere (usually the left one). Children mostly benefit from surgery due to brain plasticity, which may facilitate pre- and post-surgical reorganization, and seizure cessation may promote cognitive development. However, dominant temporal lobe resections can produce additional post-operative deficits in verbal learning and memory. Risk factors for post-operative VEM decline include ipsilesional dominance for verbal memory and language (typical in patients with left TLE), older age at seizure onset and older age at surgery. In addition, intact VEM pre-operatively is also a predictor of post-surgical VEM decline, although patients with better baseline memory will continue to have better memory post-operatively compared to those who already show impairment at baseline [20]. When looking at sex differences, some authors state that females have an advantage in VEM due to a sex-specific form of cognitive reserve that allows them to better compensate for brain pathology and maintain normal cognitive performance [23].

VEM is highly involved in school learning processes, and that is why, as pediatric neuropsychologists, we believe that further research is required on how epileptic seizures and epilepsy surgery affect this cognitive domain. We consider that it is essential to continue studying the cognitive functioning of the child's brain, based on theories focused on neurodevelopment and not on postulates based on adult neuropsychology, which has nothing to do with the formation, organization and location of cognitive functions in a vulnerable maturing brain.

The present study sets out to analyze the VEM performance among a sample of pediatric patients undergoing TLE surgery. The main objective is to determine whether the laterality of epilepsy is a major predictor for post-surgical VEM prognosis. This research also aims to shed some light on VEM relationship with other relevant demographical and clinical factors such as sex, age at onset of seizures, age at surgery and duration of epilepsy, as well as to study the impact of pre-surgical VEM performance on post-surgical outcomes. Neuropsychological criteria described in this study may offer a background to make better clinical decisions concerning TLE surgery.

In line with Skirrow et al [6], we expect that just as with language functions, which are often less strongly lateralized after early-onset focal epilepsy, developmental plasticity and compensatory processes that are active during chronic childhood epilepsy will result in a greater VEM bilaterality than noted in adults, thus expecting no significant differences in VEM performance depending on laterality of epilepsy. Following Law et al [20], we also aim to analyze whether a good performance in VEM preoperatively is a predictor of decline after surgery.

We also believe that VEM, despite being a cognitive function typically lateralized in the left temporal region, is bound to improve also in patients with right TLE surgery due to seizure reduction/release and withdrawal of administration of antiseizure medications.

Patients and methods

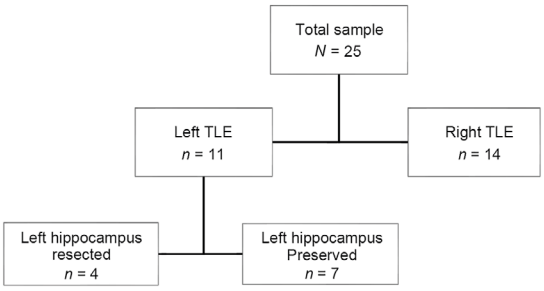
Procedure and participants

Our research was carried out in the Hospital Sant Joan de Déu (Barcelona, Spain), which has more than 150 years of history and is currently one of Europe's leading centers for maternal and child care. It is relevant to note that the present study followed a non-experimental design, as the patients' clinical data were extracted and analyzed retrospectively. After meeting the requirements established by the hospital's research bioethics committee, all clinical reports and data of the patients who underwent TLE surgery in the epilepsy unit of the hospital between 2005 and 2021 were analyzed in order to verify their suitability for the study, It is noteworthy to highlight that the inclusion criteria defined in our study were set with the aim of guaranteeing a noticeable homogeneous sample and a consequent analysis without major biases. The inclusion criteria were as follows: patients who had been diagnosed with drug refractory unilateral TLE and who underwent epilepsy surgery, with no previous surgical brain interventions. They also had to have a pre-operative and a one-year follow-up post-operative neuropsychological report, which included their general ability and VEM performance. Altogether, only 25 patients met the inclusion criteria for the study. Demographic and clinical data of the whole gathered sample is summarized in table I, Data related to each patient is also provided in table II. Note that the duration of epilepsy was defined as the period between the onset of seizures and the surgery.

Due to the nature of the study, the sample was split into two groups according to the laterality of epilepsy (Fig. 1) as a way to analyze the pre-surgical intergroup differences and the pre- to post-operative intragroup changes regarding VEM performance, as well as to explore the impact on VEM that other relevant factors might have depending on laterality.

The patients with left TLE (L-TLE group) constituted the main group of interest, as left TLE is more likely to result in memory deficits since we know that VEM is normally located in the left temporal lobe in an adult brain. The patients with right TLE (R-TLE group) served as comparison group. Performance changes after surgery were also analyzed for the whole sample. It is important to note that three patients with multifocal epilepsy that had one of the epileptics focuses in the left temporal lobe were included in the L-TLE group, and a patient with multifocal epilepsy that had one of the epileptic focuses in the right temporal lobe was included in the R-TLE group, thus maintaining a dichotomous approach (left or right temporal lobe affected). Special attention was also paid to the patients whose left hippocampus was resected at surgery, and they were compared with those who had the left hippocampus preserved.

Figure 1. Group designs. TLE: temporal lobe epilepsy.



Neuropsychological assessment

The general ability measure was obtained from the age-appropriate Wechsler intelligence scale, the Wechsler intelligence scale for children (for patients up to 16 years old) or the Wechsler adult intelligence scale (for those aged 16 and older). General ability was used as a control variable in order to ensure that VEM performance variation after surgery was not related to a sharp change in global cognitive performance. VEM scores were extracted from the España-Complutense verbal learning test for children (for patients up to 16 years old) or the España-Complutense verbal learning test (for those aged 16 and over), a word learning test which is considered the Spanish adaptation of the California verbal learning test. This test aims to assess the performance of the learning and memory system and to determine whether any of its components are fail-

Table I. Demographic and clinical data of the total sample.

N	25
Sex: male/female	11 (44%)/14 (56%)
Handedness: left/right	4 (16%)/21 (84%)
Age at onset (years)	7.25 ± 4.53
Age at surgery (years)	13.4 ± 3.85
Duration of epilepsy (years)	6.15 ± 4.33
Location of epilepsy: temporal[a]	25 (100%)
Laterality of epilepsy: left/right	11 (44%)/14 (56%)
Etiology of epilepsy:	
Tumor	7 (28%)
Dysplasia	6 (24%)
Hippocampal sclerosis	1 (4%)
Others[b]	11 (44%)
Type of surgery:	
Lesionectomy	17 (68%)
Lobectomy	2 (8%)
Anteromedial temporal resection (AMTR)	2 (8%)
Amygdalohippocampectomy (AHC)	1 (4%)
Others[c]	3 (12%)
Hippocampus resection: left/right /preserved	4 (16%)/4 (16%) /17 (68%)
Engel scale (one-year post-operative):	
IA	18 (72%)
IB	2 (8%)
ID	3 (12%)
IIIA	2 (8%)

[a] Four unilateral multifocal epilepsies were included: T-O (two), T-F (one), T-P-O (one), [b] Tumor and dysplasia (nine), dysplasia and hippocampal sclerosis (one), dysplasia and hamartoma (one), [c] Lesionectomy and lobectomy (one), lobectomy and AMTR (one), AMTR and AHC (one).

ing. It allows the assessment of the learning curve, learning stability, short- and long-term retention of information, use of learning strategies and susceptibility to interference.

The indexes whose scores were extracted for later analysis were as follows: total learning, short-term free recall and long-term free recall. The total learning raw score is the sum of words recalled over five consecutive trials, where each trial represents an attempt to recall a 15-word list (list A) after exposure. The short-term free recall raw score is determined by counting the number of words recalled after the five trials, with an additional trial in between, where interference is introduced with a different 15-word list (list B). The long-term free recall raw score is defined as the number of words recalled from the list A 15 minutes after performing the short-term memory trial.

All raw scores from the neuropsychological assessment were standardized (mean = 100; standard deviation = 15) before undergoing statistical processing.

Statistical analysis

All statistical analyses were conducted using IBM SPSS 26. A mixed model approach was employed, integrating both longitudinal assessments (from pre- to post-operative phases) and cross-sectional comparisons (Fig. 2). Bivariate correlation techniques, including Pearson and Spearman methods, were utilized to assess the relationship between two quantitative variables. Group comparisons were performed using the independent samples *t*-test, while changes within the same group from pre- to post-operative assessments were analyzed using the paired samples *t*-test. Cohen's *d* was employed to quantify the effect size for intergroup differences and intragroup changes. Visual representation of the data, such as scatter plots with fit lines or bar plots, complemented the numerical results, aiding in the visualization of trends. An alpha level of 0,05 (two-sided) was assumed for all analyses.

Results

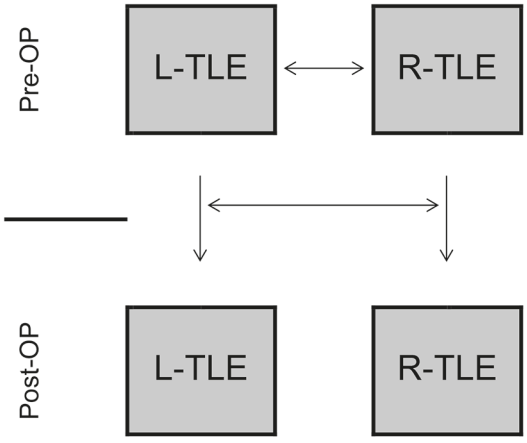
The standardized scores obtained from the neuropsychological assessment are presented below for the entire sample size and for each of the groups separately (L-TLE and R-TLE) (Table III). The variable 'Variation' was defined as the difference between the pre- and the post-operative score.

Table II. Demographic and clinical data related to each patient.

ID	Sex	Handednes	Onset age (years)	Surgery age (years)	Duration (years)	Location	Laterality	Etiology	Surgery type	Hippocampus resection	Engel scale (one-year post-operative)
1	M	R	13.25	14.1	0.85	T	R	Tumor	Lesionectomy	Preserved	IA
2	F	L	0.5	11.58	11.08	T	L	Tumor	AHC	L	IB
3	F	R	7	10.44	3.44	T	R	Tumor and dysplasia	Lesionectomy	R	IA
4	M	R	7	7.44	0.44	T	L	Dysplasia and hamartoma	Lesionectomy	Preserved	IA
5	F	R	10	15.39	5.39	T	R	Tumor and dysplasia	Lesionectomy	Preserved	ID
6	M	R	13	17.12	4.12	T	R	Tumor and dysplasia	AMTR	R	IA
7	F	R	5	7.67	2.67	T	L	Dysplasia	AMTR	L	IA
8	M	R	6	14.03	8.03	T	R	Dysplasia	Lesionectomy	Preserved	ID
9	F	R	10	11.96	1.96	T	R	Dysplasia	Lesionectomy	Preserved	IIIA
10	F	R	3	15.67	12.67	T	L	Dysplasia	Lobectomy	Preserved	IA
11	M	R	11	16.51	5.51	T	L	Tumor and dysplasia	Lesionectomy	Preserved	IA
12	F	R	9	12.08	3.08	T-F	L	Tumor	Lesionectomy	Preserved	ID
13	F	R	13	18.2	5.2	T-O	R	Tumor and dysplasia	Lesionectomy and lobectomy	Preserved	IA
14	F	R	1	7.49	6.49	T	R	Tumor	Lesionectomy	Preserved	IA
15	F	R	13	17.17	4.17	T	R	Tumor and dysplasia	Lesionectomy	Preserved	IA
16	M	R	9	17.63	8.63	T	R	Dysplasia, and hippocampal, sclerosis	Lobectomy	R	IA
17	F	R	3	10.93	7.93	T	L	Tumor	Lesionectomy	Preserved	IB
18	F	R	8	9.37	1.37	T	R	Tumor and dysplasia	Lesionectomy	Preserved	IA
19	M	R	16.92	17.64	0.72	T	R	Tumor and dysplasia	Lesionectomy	Preserved	IA
20	M	L	2.33	19.82	17.49	T	R	Dysplasia	AMTR and AHC	R	IA
21	F	R	3	7.91	4.91	T-O	L	Tumor and dysplasia	Lobectomy, and AMTR	L	IA
22	M	R	7	13.16	6.16	T	R	Tumor	Lesionectomy	Preserved	IA
23[a]	F	R	6	18.78	12.78	T	L	Hippocampal sclerosis	Lesionectomy	L	IA
24	M	L	3.67	11.2	7.53	T	L	Tumor	Lesionectomy	Preserved	IA
25	M	L	0.67	11.8	11.13	T-P-O	L	Dysplasia	Lesionectomy	Preserved	IIIA

AHC: amygdalohippocampectomy; AMTR: anteromedial temporal resection; F: female; L: left; M: male; O: occipital; P: parietal; R: right; T: temporal. [a] The posterior part of the left hippocampus was spared in the resection.

Figure 2. Mixed model approach followed for the statistical analysis. L-TLE: left temporal lobe epilepsy; pre-OP: pre-operative; post-op: post-operative; R-TLE: right temporal lobe epilepsy.



Pre-operative analysis

Effect of laterality
No significant pre-surgical differences in performance were found between the L-TLE and the R-TLE groups for any VEM index (for all indexes, $p > 0.52$).

Effect of sex
Sex showed no significant impact on pre-operative VEM scores when analyzing the entire sample, composed of 11 males and 14 females (total learning: $t = 1.61$, $p = 0.12$, $d = 0.65$; short-term free recall: $t = 0.41$, $p = 0.68$, $d = 0.17$; long-term free recall: $t = 1.57$, $p = 0.13$, $d = 0.63$).

Effect of age at onset
Looking at the L-TLE group, a low negative correlation was found between the onset age and the pre-operative total learning score (rho = –0.44, $p = 0.18$), but not quite significant. Also a moderate negative correlation was found between the onset age and the pre-operative short-term free recall score (rho = –0.55, $p = 0.08$), but still not statistically significant. Lastly, a high negative correlation, statistically significant this time, was found between the onset age and the pre-operative long-term free recall score (rho = –0.72, $p = 0.01$). On the other hand, looking at the R-TLE group, low and not significant positive correlations were found between the onset age and pre-operative scores (total learning: $r = 0.30$, $p = 0.30$; short-term free recall score: $r = 0.15$, $p = 0.62$; long-term free recall: $r = 0.22$, $p = 0.45$). Scatter plots (Figs. 3 and 4) illustrate the comparison between the two groups, only for the long-term free recall index.

Post-operative analysis

General ability
The results showed that general ability did not vary significantly in the whole sample ($p = 0.88$) nor in the two groups separately (L-TLE group: $p = 0.89$; R-TLE group: $p = 0.95$).

VEM
No significant performance changes were found when looking at the total sample (for all VEM indexes, $p > 0.23$) nor in the two groups separately (L-TLE group: for all VEM indexes, $p > 0.56$; R-TLE group: for all VEM indexes, $p > 0.12$).

Effect of left hippocampus resection
In average terms, the patients whose left hippocampus was resected experimented a small additional decline after surgery in all VEM indexes, whereas those who had their left hippocampus preserved experimented a very slight improvement (also in all VEM indexes), but these intergroup differences did not reach enough statistical significance (for all VEM indexes, $p > 0.06$).

Effect of age at surgery and duration of epilepsy
Looking at the L-TLE group, surgery age did not show a significant impact on pre- to post-operative score variations for any VEM index (for all indexes, $p > 0.33$). However, in the R-TLE group, surgery age showed to have a negative moderate correlation with the long-term free recall score change ($r = –0.56$, $p = 0.04$; for total learning and short-term free recall, $p > 0.17$). The duration of epilepsy was shown to be an irrelevant factor regarding performance changes after surgery (for all VEM indexes in both groups, $p > 0.55$).

Effect of pre-operative VEM performance
To examine the impact of pre-operative VEM performance on changes after surgery, the L-TLE group patients were separated into two subgroups or categories according to their pre-surgical long-term free recall performance: impaired (pre-operative long-term free recall score below 85) or not impaired (pre-operative long-term free recall score equal or above 85). The results showed that the patients with unimpaired pre-operative performance

Table III. Standardized scores obtained from the neuropsychological assessment –M ± SD (min, max)–.

Total sample (*N* = 25)	Pre-operative	Post-operative	Variation (post-operative — pre-operative)
General ability	89.4 ± 14.77 (55, 113)	89.16 ± 15.12 (55, 118)	–0.24 ± 8.06 (–17, 12)
Total learning	93.84 ± 13.22 (68, 120)	97.12 ± 16.48 (70, 130)	3.28 ± 15.93 (–30, 37)
Short-term free recall	91.36 ± 16.31 (55, 115)	95.56 ± 16.89 (63, 123)	4.2 ± 17.5 (–30, 30)
Long-term free recall	92.96 ± 18.38 (55, 123)	96.28 ± 19.11 (55, 123)	3.32 ± 15.4 (–37, 38)
Left TLE (*n* = 11)	**Pre-operative**	**Post-operative**	**Variation (post-operative — pre-operative)**
General ability	86.27 ± 15.01 (59, 111)	85.91 ± 10.49 (67, 105)	–0.36 ± 8.67 (–15, 11)
Total learning	94.27 ± 12.46 (78, 120)	92.09 ± 12.28 (72, 115)	–2.18 ± 12.42 (–30, 11)
Short-term free recall	89 ± 11.58 (70, 106)	91.64 ± 15.1 (63, 112)	2.64 ± 16.87 (–30, 30)
Long-term free recall	93.64 ± 17.80 (70, 123)	94 ± 15.94 (69, 115)	0.36 ± 18.38 (–37, 23)
Right TLE (*n* = 14)	**Pre-operative**	**Post-operative**	**Variation (post-operative — pre-operative)**
General ability	91.86 ± 14.65 (55, 113)	91.71 ± 17.93 (55, 118)	–0.14 ± 7.88 (–17, 12)
Total learning	93.5 ± 14.25 (68, 115)	101.07 ± 18.64 (70, 130)	7.57 ± 17.45 (–23, 37)
Short-term free recall	93.21 ± 19.49 (55, 115)	98.64 ± 18.12 (70, 123)	5.43 ± 18.52 (–30, 30)
Long-term free recall	92.43 ± 19.47 (55, 123)	98.07 ± 21.71 (55, 123)	5.64 ± 12.9 (–15, 38)

max: maximum; min: minimum; TLE: temporal lobe epilepsy.

tended to experience a long-term free recall decline after surgery, while the patients with already impaired pre-operative performance tended to show improvement, reporting a large effect size for these differences between both subgroups, although a very slight trend toward significance (t = 1.37, p = 0.20, d = 0.86). The average change of the long-term free recall score depending on the pre-surgical long-term free recall performance is illustrated in figure 5.

Discussion

The current study assessed VEM performance in a monocentric series of children and adolescents undergoing TLE surgery. The analysis considered the neuropsychological status before surgery and one year after surgery. Our major aim was to determine whether the laterality of epilepsy could be a crucial factor to be considered in pediatric TLE surgery with regard to post-operative VEM prognosis. As secondary objectives, we also studied the effect on VEM of other relevant demographic and clinical factors such as sex, age at onset of seizures, age at surgery and duration of epilepsy, as well as the impact of pre-surgical VEM performance on post-surgical outcomes.

Most of the results were not statistically significant in our primary analyses, probably due to the relatively small sample size, but we could find interesting trends that were consistent with previous studies about this issue.

Pre-operative analysis

The present data showed no significant differences in pre-operative VEM performance between pa-

Figure 3. Left temporal lobe epilepsy group (n = 11). Scatter plot with fit line: pre-operative long-term free recall score by onset age (years). LTFR: long-term free recall; pre-OP: pre-operative.

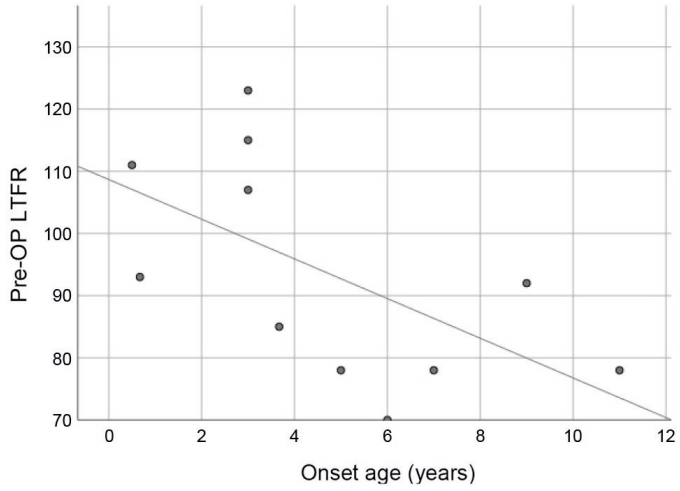
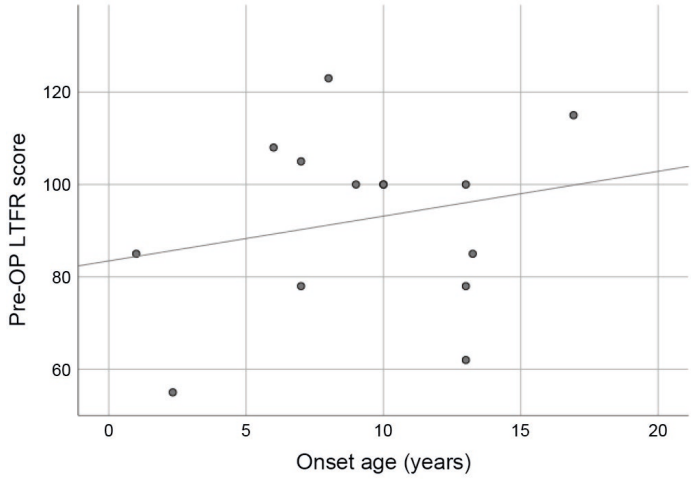


Figure 4. Right temporal lobe epilepsy group (n = 14). Scatter plot with fit line: pre-operative long-term free recall score by onset age (years). LTFR: long-term free recall; pre-OP: pre-operative.



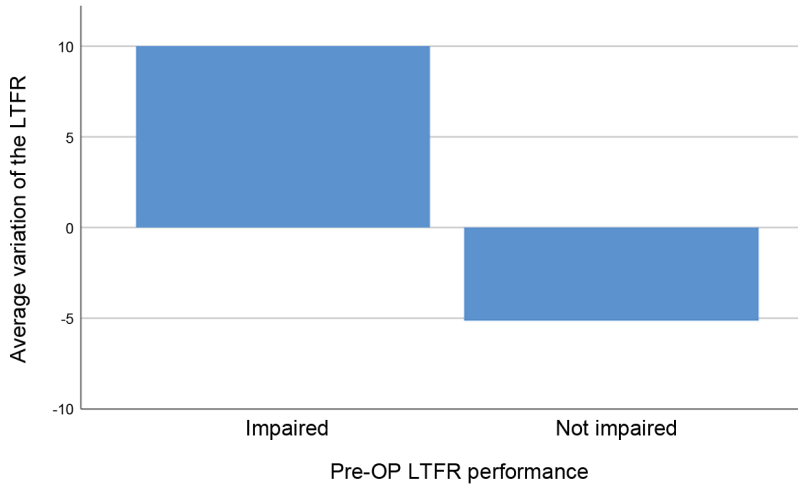
tients with left- and right-sided TLE in our sample, fact that supports the hypothesis of bilateral memory representation when seizures begin at early ages, in view of a low average onset age (7.25 years) in our sample that may have caused the patients with epileptic focus in the left hemisphere to partially consolidate their VEM in the contralesional hemisphere. In accordance with the previously mentioned considerations, onset age showed a high negative correlation (rho = –0.72, p = 0.01) with the long-term free recall score only when TLE was left-sided. It is quite evident that a very early onset age is cognitively detrimental in a broad sense, due to early seizures and administration of the administration of antiseizure medications, which may damage the brain at a very vulnerable stage of its development. However, the same is not true when it comes to the performance in some very localized cognitive functions, such as VEM; as has been shown in previous studies, as well as in our own, a younger age at seizure onset seems to be beneficial for the consolidation of this function in the contralesional hemisphere, likely due to a more efficient reorganization of memory system induced by a greater brain plasticity at lower ages. This finding reflects once again the 'plasticity vs. vulnerability' issue, where the focality of the lesion/epilepsy and the age of the child at the time of the seizure onset will be of major relevance for the neuropsychological prognosis. Although the p-value did not reach the established cut-off point, probably due to a lack of statistical power, females showed an evident trend to perform moderately better than males in long-term free recall (t = –1.57, p = 0.13, d = 0.63), in line with recent bibliography [23], and with a larger sample size that trend would probably be significant and somewhat substantial assuming the effect size was maintained.

Post-operative analysis

Seizure control was good with 72% of all operated children being completely seizure free (Engel IA) one year after surgery, a percentage very similar to that described by Ramantani and Reuner [7]. On a group level, no significant decline or improvement in VEM performance was found one year after surgery neither in the overall sample nor in the left or right temporal surgeries separately. Nevertheless, the patients who underwent left hippocampus resection showed a small additional decline after surgery, whereas a very slight improvement was found in those patients whose hippocampal structures were spared; these results did not reach enough statistical significance, though, likely due to a small sample size. Regarding right TLE, surgery age showed to be a predictor related to post-operative changes in long-term free recall performance (r = –0.56, p = 0.04); the improvement in a year's follow-up was greater as the patients underwent surgery earlier, probably due to a younger age at the

time of seizures release/reduction and withdrawal of the administration of antiseizure medications that may have enhanced cognitive development, following Skirrow et al [6]. On the other hand, when looking at left-sided TLE, an early age at surgery did not prove to be a key factor for VEM improvement after surgery, as opposed to Law's et al [20] statements. At last, intact pre-operative VEM showed a slight slide towards significance (t = 1.37, p = 0.20, d = 0.86) to be a risk factor for post-operative decline, in line with Law's et al [20] study. However, it is difficult to determine whether this is due to an asymptotic effect of the neuropsychological tests, so we should interpret the results with caution.

Figure 5. Left temporal lobe epilepsy group (n = 11). Average variation of the long-term free recall score by presurgical long-term free recall performance. LTFR: long-term free recall.



Conclusions

Overall, our results are quite consistent with previous studies about this topic. Before surgery there seems to be no differences in VEM performance between patients with left- and right-sided TLE, likely due to a bilateral memory representation when seizures begin at early development stages. Furthermore, only when epilepsy is left-sided, a younger age at onset of seizures shows to lead to a better pre-operative performance, probably due to a more efficient reorganization of memory system induced by a greater brain plasticity at lower ages. At one-year follow-up, TLE surgery in pediatric ages does not appear to lead to either a decline or an improvement in VEM outcome, regardless of epilepsy laterality. However, the results suggest that left TLE surgery is more likely to cause an additional VEM decline when the resection involves the left hippocampus, thus according to previous bibliography. The post-surgical performance improvement in right TLE seems to be greater the earlier patients undergo surgical intervention, probably due to a younger age at the time of seizures release/reduction and withdrawal of the administration of antiseizure medications that may enhance cognitive development. At last, patients with an average or above average pre-operative performance in VEM tasks appear to have an increased risk for further post-operative decline, also in line with previous research.

Limitations and future directions

- The main shortcomings of the present study are the retrospective approach and the small sample sizes, The authors are well aware that non-randomized studies like the present bear a high risk of bias. Future studies will likely require a multicenter collaboration in order to recruit a larger sample of children that will allow for a more accurate inferential analysis.
- Each patient with epilepsy in our sample has unique characteristics (e.g., underlying pathology or seizure type, frequency, and duration), making it challenging to form a homogeneous group.
- Due to variability in underlying pathology, it is crucial to acknowledge that surgical procedures are not uniform and may result in variable sparing of the temporal lobe and hippocampal structures. Unfortunately, data on the amount of excised tissue during surgery were not available.
- We were unable to analyze whether the reorganization of the VEM system might result in a decline in visual memory due to a saturation effect, as it was not feasible to extract visual memory scores from all the patients in our sample. As a future avenue of exploration, it would be interesting to examine whether such a saturation effect could occur as a consequence of this brain plasticity phenomenon.
- Language lateralization is assumed to be typical in our sample. However, making thi–s assumption entails some risk of bias because some patients, especially those who are left-handed, might have language lateralized in the right hemisphere or shared across both hemispheres.

– All the patients in our sample were undergoing polytherapy with the administration of antiseizure medications. The drug administration may have adversely impacted attention and processing speed, thereby modulating performance in VEM. Neuropsychological tests do not allow for a pure assessment of the cognitive domain we aim to evaluate, as cognitive functions overlap and they cannot be assessed in isolation. Hence, caution is warranted when interpreting the results.
– More extensive follow-up may be required to establish the full impact of surgery on VEM.
– An over-interpretation of our findings should be avoided. Our findings come from group analysis, and extrapolation to individual patients in a clinical or surgical setting might be problematic.

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Memoria episódica verbal en pacientes pediátricos intervenidos de cirugía de la epilepsia del lóbulo temporal: un estudio de seguimiento al año

Introducción. La memoria episódica verbal (MEV) no suele resultar alterada en niños con epilepsia focal sometidos a resecciones del lóbulo temporal izquierdo, a diferencia de lo que cabría esperar si se tratara de un cerebro adulto. Los últimos hallazgos sugieren que la actividad epileptógena en los primeros años de vida disrumpe la lateralización del sistema mnésico, lo que conduce al desarrollo de una representación bilateral de la memoria. El presente estudio pretende analizar si la lateralidad de la epilepsia es un predictor significativo de cara al pronóstico posquirúrgico de la MEV en la cirugía de la epilepsia del lóbulo temporal (ELT) en edad pediátrica. Esta investigación también pretende aportar evidencias sobre la relación de la MEV con otros factores demográficos y clínicos relevantes, como el sexo, la edad de inicio de las crisis, la

edad quirúrgica y la duración de la epilepsia, así como estudiar el impacto del rendimiento prequirúrgico en la MEV sobre los resultados posquirúrgicos.

Pacientes y métodos. Se extrajeron de la base de datos del Hospital Sant Joan de Déu y se analizaron retrospectivamente las puntuaciones prequirúrgicas y al año de seguimiento postoperatorio de una tarea de recuerdo de lista de palabras correspondientes a 25 niños intervenidos de ELT (ELT izquierdo, $n = 11$; ELT derecho, $n = 14$).

Resultados. No se encontraron diferencias intergrupales prequirúrgicas significativas al comparar las puntuaciones en MEV sobre la base de la lateralidad de la epilepsia ($p > 0,5$). En cuanto al grupo de ELT izquierdo, se encontró una alta correlación negativa entre la edad de inicio y la puntuación prequirúrgica del recuerdo libre a largo plazo (rho = –0,72; $p = 0,01$). No se encontraron cambios intragrupo significativos entre el pre- y el postoperatorio en relación con el rendimiento en la MEV, independientemente de la lateralidad de la epilepsia (grupo de ELT izquierdo, $p > 0,56$; grupo de ELT derecho, $p > 0,12$).

Conclusiones. La lateralidad de la epilepsia no parece ser un factor significativo por sí solo en relación con el rendimiento prequirúrgico en la MEV y su pronóstico un año después de la cirugía, lo que apoya la hipótesis de una representación bilateral de la memoria. Además, una edad más temprana al inicio de las crisis parece estar relacionada con un mejor resultado preoperatorio en la MEV, probablemente debido a una reorganización más eficiente del sistema de memoria inducida por una mayor plasticidad cerebral en edades más bajas; sin embargo, esta relación sólo se ha observado en nuestra muestra para las epilepsias de lateralidad izquierda.

Palabras clave. Epilepsia farmacorresistente. Epilepsia del lóbulo temporal. Hospitales pediátricos. Memoria episódica. Neurocirugía. Plasticidad neuronal.